Dorzolamide Restores Choroidal Blood Flow in the DBA/2J Mouse Model of Glaucoma

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PURPOSE: Dorzolamide (DZ) is clinically used to treat glaucoma by reducing intraocular pressure. However, its effect on blood flow is unknown. The goal of this study is to investigate the effect of topical DZ application on retinal and choroidal blood flow in DBA/2J mice, an established mouse model of glaucoma. Results are compared with C57BL/6J mice, used as a control group.

METHODS: All methods were performed according to IACUC guidelines. C57BL/6J mice (n=2) aged 4 months and DBA/2J (n=2) mice aged 4 and 7 months respectively were used for the in vivo MRI study. The animal holder had ear and tooth bars to minimize motion. The animal was anesthetized, respiration monitored (80-110 bpm) and temperature was maintained at 37°C using a warm water circulation pad. The heart rate and O₂ saturation were also monitored. MRI scans were performed in a 7T magnet (Bruker Biospec, Billerica, MA) with a 150 Gauss/cm gradient using a custom eye coil for imaging (diameter, 6 mm) and a heart coil for ASL (diameter, 8 mm) as described in [1]. The BF scans were acquired with a gradient-echo, echo-planar imaging sequence with a 6 mm x 6 mm field of view and a 144 x 144 matrix zero-filled interpolation to 256x256. The BF sequence used a single, 400 μm coronal slice, 2 shots, 2.94-second labeling pulse, 3.0 second repetition time, and 9.8 ms echo time. The slice was positioned near the optic nerve and tilted to be perpendicular to the retina. BF values were calculated from images acquired over a 20-minute period and were averaged offline. Once the initial scans were acquired (before treatment), a single drop (5 μl) of Dorzolamide HCL Ophthalmic Solution, 2% (Bausch+Lomb™) was applied on the eye. Subsequent post DZ scans were acquired using the same setup.

RESULTS: The retina was linearized by radially projecting the profiles (blue lines) along the retina as shown in Fig. 1A. This resulted in blood flow peaks as shown in Fig 1B. The retinal and choroidal vascular layers were distinctly resolved and values were noted. The two groups (C57BL/6 and DBA/2J) were imaged before as well as (~1.5 Hr) after DZ treatment. Post DZ treatment, we observed a statistically significant (p<0.05) increase in blood flow in both groups in the choroid. The blood flow changes in the retina were however not statistically significant (data not shown).

DISCUSSION AND CONCLUSIONS: This study indicates that topical Dorzolamide administration increased choroid blood flow but not retinal blood flow in both DBA/2J glaucoma mice and normal controls. DZ is a carbonic anhydrase inhibitor which is known to have vasodilatory effects [2]. Future studies will investigate chronic DZ administration and at different stages of the disease.